PERRIGO®

May 3, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

99 MAY -7 P1:36

Re: Draft Guidance for Industry
ANDAs: Impurities in Drug Products
Docket No. 98D-1168

Dear Sir or Madam:

Perrigo Company respectfully submits these comments in response to the Food and Drug Administration's "Draft Guidance for Industry ANDAs: Impurities in Drug Products", Docket No. 98D-1168. In general, we do not object to the contents of the draft guidance document, which will assist companies in defining the required impurities testing of drug products.

Perrigo is the nation's largest private-label manufacturer of over-the-counter drug products, serving numerous chain drugstores and supermarkets. Most of these OTC products are marketed under OTC monographs. Many of Perrigo's drug products are covered by approved abbreviated new drug applications (ANDAs), which must include impurities testing of drug substances and products.

I. INTRODUCTION:

Line 8 — This sentence should replace the term "other impurities" with "reaction products" so that it is not misinterpreted as impurities due to the synthetic process of the active substance.

Line 15 — The term "related" to USP monograph should be clarified. It should be stated whether a drug product not specifically covered by a monograph but 'related' to a monograph product would need to follow an impurity specification for the monograph product. For example, a non-monographed two active ingredient generic product for which there exist monographs covering each single component product.

Line 33 — If an active pharmaceutical ingredient manufacturer included in an ANDA uses a synthetic process which is different from that used by the RLD, is the ANDA applicant required to provide results of toxicological studies performed by the ingredient manufacturer?

Line 34 — It is stated that "Although generic drug products are not covered by Q3B, many of the recommendations in QB3 are applicable to generic drug products." Please clarify whether there are any recommendations in Q3B that are applicable to generic drug products that are not included in this draft guidance.

98D-1168 C13

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II. CLASSIFICATION OF IMPURITIES:

Line 41 Does this definition include second order reaction products, i.e. degradation products from degradation products?

Line 55 Will there be a separate document which will address impurities arising from excipients?

III. IDENTIFYING AND REPORTING IMPURITIES:

Line 90 It is not clear whether the retention time matching of a degradant peak in the generic drug's chromatogram with that of the RLD is sufficient to "identify" the impurity. It should be enough to confirm that it is the same compound (if reference standards are not available). Clarify that the ANDA applicant will not be required to identify what the compound is if it is present in similar amount as the RLD.

IV. ANALYTICAL PROCEDURES:

Line 95 "should be identified" should be changed to "should make a reasonable effort to identify" by using these techniques.

V. REPORTING IMPURITY CONTENT IN BATCHES:

No comments.

VI. ACCEPTANCE CRITERIA FOR IMPURITIES:

No comments.

VII. QUALIFYING IMPURITIES:

Line 215 ANDA applicants cannot determine the date of manufacture of RLD products, although the date may be estimated from the expiration date on the marketed package.

VIII NEW IMPURITIES:

No comments.

Perrigo appreciates the opportunity to submit these comments. If you have any questions, please feel free to call me at 616-673-9745.

Sincerely,

PERRIGO COMPANY

Brian R. Schuster
Manager, ANDA Submissions

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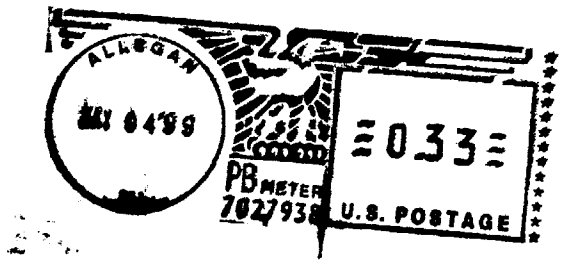

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